Claims

1. A method for treating neurodegenerative diseases or disorders comprising the administration to a patient of a first compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, wherein said first compound is administered simultaneously with, separate from or prior to the administration of a second compound to said patient to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said second compound.

2. The method of claim 1, wherein said first compound is pipamperone.

3. The method of claim 2, wherein said first compound is administered to a patient in a dose ranging between 5 and 15 mg of the active ingredient.

4. The method of any of claims 1 to 3, wherein said neurodegenerative disease or disorder is Parkinson Disease.

5. The method of any of claims 1 to 4, wherein said first compound is administered daily at least one day before administering said second compound.

6. The method of any of claims 1 to 5, wherein said second compound is a dopamine receptor agonist.

7. The method of claim 6, wherein said dopamine receptor agonist is chosen from the group consisting of amantadine, bromocriptine, cabergoline lisuride, pergolide, ropinirole and pramipexole, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

8. The method of claim 7, wherein said dopamine receptor agonist is pergolide and is administered in a dose ranging between 0.5 and 10 mg of the active ingredient.

9. A pharmaceutical composition comprising

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A

receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors and

(b) a dopamine receptor agonist,

as a combined preparation for simultaneous, separate or sequential use for treating a neurodegenerative disease or disorder such as Parkinson Disease.

10. The method of any of claims 1 to 5, wherein said second compound is levodopa associated with a decarboxylase inhibitor.

11. The method of claim 10, wherein said levodopa/decarboxylase-inhibitor is chosen from the group consisting of levodopa/carbidopa and levodopa/benserazide, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

12. The method of claim 12, wherein said levodopa/decarboxylase-inhibitor is levodopa/carbidopa and is administered in a dose ranging between 2000 mg/ 200 mg and 100 mg/ 10 mg of the active ingredients.

13. A pharmaceutical composition comprising

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(b) a levodopa associated with a decarboxylase inhibitor,

as a combined preparation for simultaneous, separate or sequential use for treating a neurodegenerative disease or disorder such as Parkinson Disease.

14. The method of any of claims 1 to 5, wherein said second compound is a mono-amine oxidase B (MAO-B) inhibitor.

15. The method of claim 14, wherein said second compound is selegilinehydrochloride or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

16. The method of claim 15, wherein said selegilinehydrochloride is administered in a dose ranging between 2 and 25 mg of the active ingredient.

17. A pharmaceutical composition comprising

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors and

(b) a mono-amine oxidase B (MAO-B) inhibitor,

as a combined preparation for simultaneous, separate or sequential use for treating a neurodegenerative disease or disorder such as Parkinson Disease.

18. A method for treating a neurodegenerative disease or disorder comprising the administration to a patient of (a) a first compound having a selective affinity for the D4 receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, (b) a second compound having a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and (c) a third compound, wherein the administration of said first and second compounds is simultaneously with, separate from or prior to the administration of said third compound to said patient to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said third compound.

19. The method of claim 18, wherein said neurodegenerative disease or disorder is Parkinson Disease.

20. The method of claim 18 or 19, wherein said first compound is chosen from the group consisting of, pipamperone, fananserin, L-745,870, PNU-101387G and U-101387 or a pro-drug or a pharmaceutically acceptable salt thereof and wherein said second compound is chosen from the group comprising pipamperone, fananserin, ORG 5222, zotepine, olanzepine, clozapine, S16924, S18327, amperozide, serindole, MDL 100.907, tiospirone, fluspirilene, ocaperidone, risperidone, paliperidone and ziprasidone or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

21. The method of any of claims 18 to 20, wherein said composition is administered to a patient in a dose ranging between 0.5 μg and 2000 mg for each of the active ingredients.

22. The method of any of claims 18 to 20, wherein said third compound is a dopamine receptor agonist.

23. The method of claim 22, wherein said dopamine receptor agonist is chosen from the group consisting of amantadine, bromocriptine, cabergoline lisuride, pergolide, ropinirole and pramipexole, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

24. The method of claim 23, wherein said dopamine receptor agonist is pergolide and is administered in a dose ranging between 0.5 and 10 mg of the active ingredient.

25. A pharmaceutical composition comprising

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors,

(b) a compound having a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(c) a dopamine receptor agonist,

as a combined preparation for simultaneous, separate or sequential use for treating a neurodegenerative disease or disorder such as Parkinson Disease.

26. The method of any of claims 18 to 20, wherein said third compound is levodopa associated with a decarboxylase inhibitor.

27. The method of claim 26 wherein said levodopa/decarboxylase-inhibitor is chosen from the group comprising levodopa/carbidopa, levodopa/benserazide, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

28. The method of claim 27, wherein said levodopa/decarboxylase-inhibitor is levodopa/carbidopa and is administered in a dose ranging between 2000 mg/ 200 mg and 100 mg/ 10 mg of the active ingredients.

29. A pharmaceutical composition comprising

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and

(b) a compound having a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(c) levodopa associated with a decarboxylase inhibitor,

as a combined preparation for simultaneous, separate or sequential use for treating a neurodegenerative disease or disorder such as Parkinson Disease.

30. The method of any of claims 18 to 20, wherein said third compound is a mono-amine oxidase B (MAO-B) inhibitor.

31. The method of claim 30, wherein said mono-amine oxidase B (MAO-B) inhibitor is selegelinehydrochloride or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

32. The method of claim 31, wherein selegilinehydrochloride is administered in a dose ranging between 2 and 25 mg of the active ingredient.

33. A pharmaceutical composition comprising

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and

(b) a compound having selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors. and

(c) a mono-amine oxidase B (MAO-B) inhibitor,

as a combined preparation for simultaneous, separate or sequential use for treating a neurodegenerative disease or disorder such as Parkinson Disease.

34. A method for treating a cognitive disease or disorder comprising the administration to a patient of (a) a first compound as defined in any of claims 1 to 3, or (b) a first and a second compound as defined in claim 18, and (c) a cholinesterase inhibitor, wherein the administration of said compounds of (a) or (b) is simultaneously with, separate from or sequential to the administration to said patient of said cholinesterase inhibitor to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said cholinesterase inhibitor.

35. The method of claim 34, wherein said disease or disorder is selected from the group consisting of delirium; dementia, such as Alzheimer Disease, substance-induced persisting dementia, vascular dementia, dementia due to a general medical condition chosen from the group comprising HIV disease, head trauma, Parkinson Disease, Huntington Disease, Pick Disease and Creutzfeldt-Jacob Disease; amnestic disorders due to a general medical condition or a substance-induced persisting amnestic disorder; mild cognitive impairment disorder; and other cognitive disorders.

36. The method of claim 34 or 35, wherein said cholinesterase inhibitor is chosen from the group consisting of donepezil, ENA-713, galantamine, memantine and tacrine, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

37. The method of claim 36, wherein said cholinesterase inhibitor is galantamine and is administered in a dose ranging between 5 and 50 mg of the active ingredient.

38. A pharmaceutical composition comprising

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(b) a cholinesterase inhibitor

as a combined preparation for simultaneous, separate or sequential use for treating a cognitive disease or disorder.

39. A pharmaceutical composition comprising

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and

(b) a compound having a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(c) a cholinesterase inhibitor ,

as a combined preparation for simultaneous, separate or sequential use for treating a cognitive disease or disorder.

40. A pharmaceutical composition according to any of claims 9, 13, 17 or 38 wherein said compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, is pipamperone and is present in the composition in a dose ranging between 5 and 15 mg of active ingredient, expressed as the daily dose administered to a patient in need thereof.